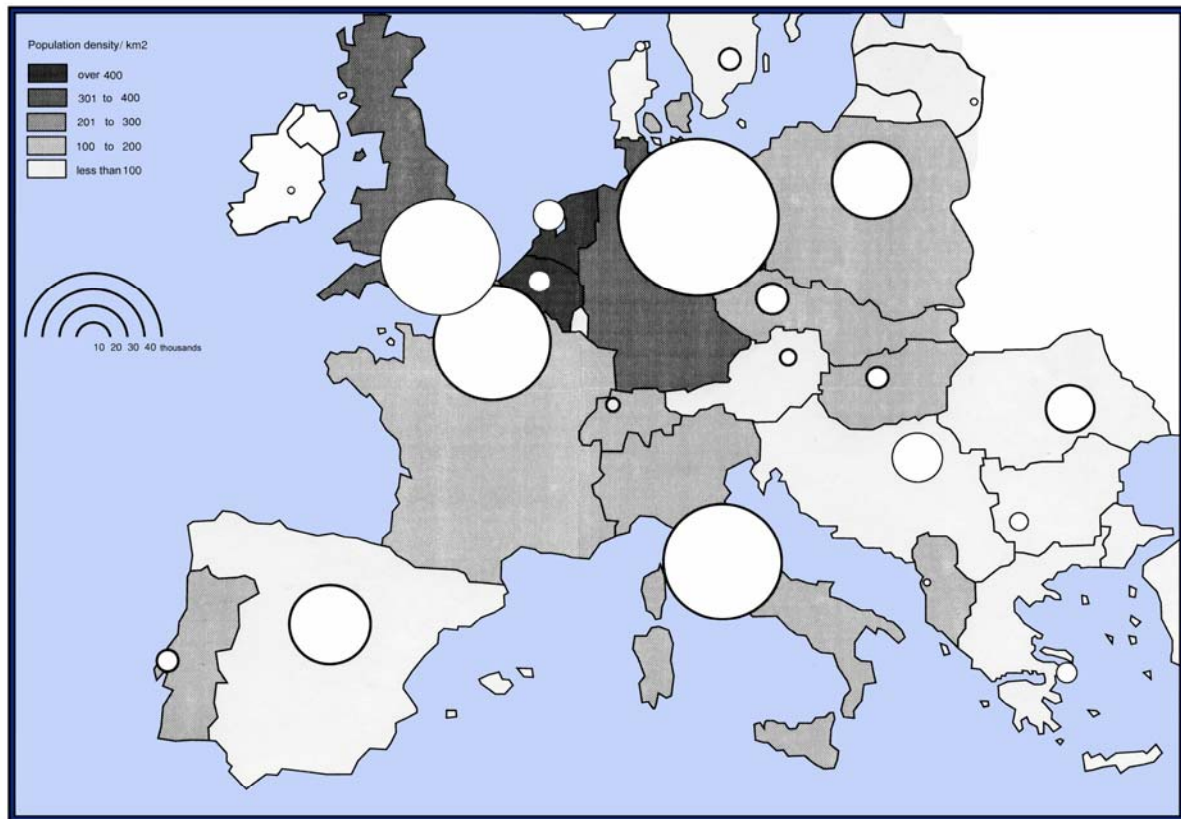


Prevalence of Inherited Retinal Dystrophies

(Retinitis pigmentosa, choroidal and macular dystrophies)



Estimated number of retinal dystrophies in Europe

Bernard Puech Exploration de la Vision et Neuro-Ophtalmologie. Hôpital Roger Salengro Lille 59037

- 1994 06 18 - Vilnius – Workshop of the CONCERTED ACTION OF THE EUROPEAN COMMUNITIES - Prevention of Blindness: Molecular Research and Medical Care -

Summary

The author presents a retrospective study made on inherited retinal dystrophies as recorded among the inhabitants of the Nord-Pas-de-Calais region, France. This study on a population of nearly 4 million inhabitants covering eighteen years has enabled us to try and assess the prevalence of each disease.

Epidemiological studies regarding inherited macular dystrophies are almost nonexistent, while we may find many on retinitis pigmentosa prevalence. A census of all groups of inherited retinal dystrophies detected in the main centre of ophthalmologic diagnosis in Northern France by the end of 1991 was taken. From this census, peripheral and central attacks were separated and incidence of each of these retinal affections was calculated.

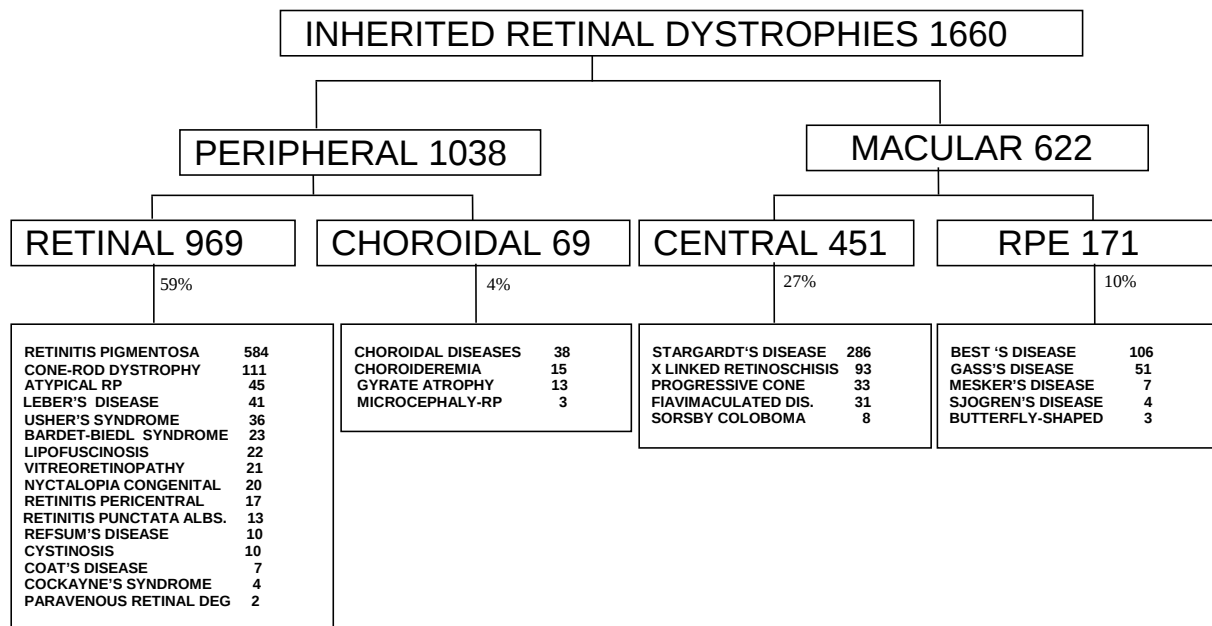


Figure 1. Inherited retinal dystrophies recorded among the inhabitants in the North of France from 1972 to 1989 (RPE: retinal pigmented epithelium).

This study is performed on patients with inherited retinal dystrophies registered at the Department of Ophthalmology of the Lille Regional University Hospital (CHRU) over a period of eighteen years (from 1972 to 1990). 1,660 inherited retinal dystrophies were detected (fig. 1). The hospital covers a population of four million inhabitants living in a geographic area called Nord-Pas-de-Calais in Northern France. The age pyramid in 1990 for all the patients concerned is represented in fig 2. The polling method used (argument poll) and the sample representativity were discussed in a previous article (Puech et al. 1991).

The age pyramid of the detected cases followed that of the population under scrutiny (fig. 2). Detection of all dystrophies increased up to the age of 35, then followed the normal decreasing pattern of the older generations. As for retinoschisis, detection usually took place in the first fifteen years after birth; for Stargardt's disease, it may have occurred up to the age of 20, and for Best's dystrophy, the process was the most extended and the slowest one to appear.

The proportion of affected patients was measured against the division of the area into districts, which enabled us to assess their geographical distribution. This distribution is connected with the population density, except for a few cases corresponding to centers of dominant inherited dystrophies situated in rural areas. 87% of the population in Northern France are native, 7% come from North Africa, 3.3% from Slavonic countries, and 2.7% from South European countries. The analysis of the distribution and inheritance of the various forms of retinitis pigmentosa confirmed the results obtained in other recent and similar studies carried out in other countries (table 1).

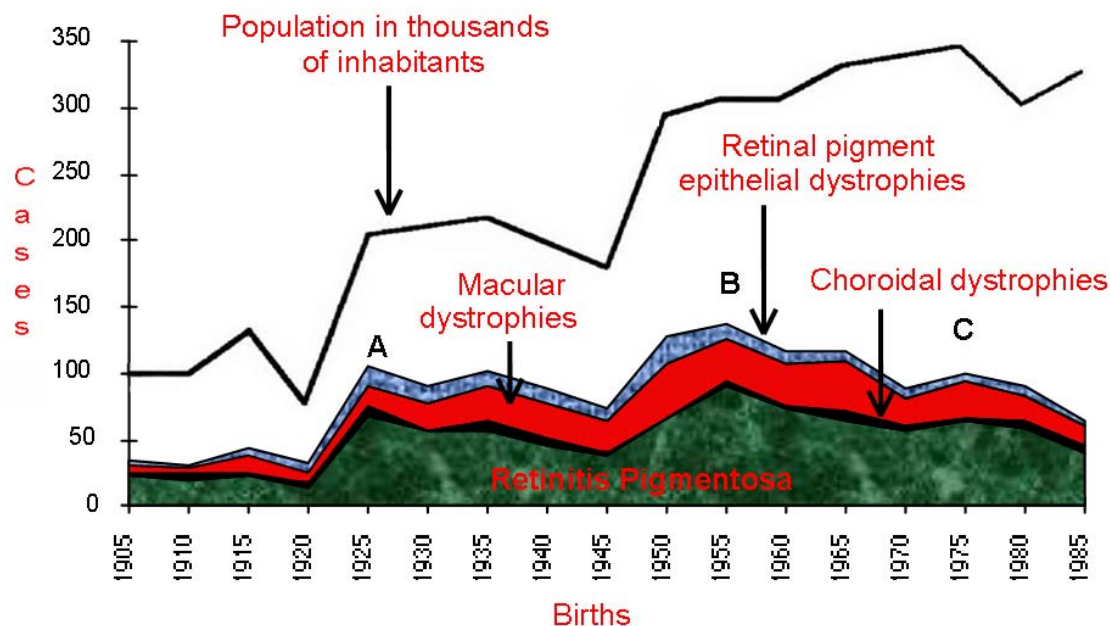


Figure 2. Age pyramid of the detected cases and age pyramid of the population.

There seemed to be a sufficient number of patients to try and assess the prevalence of inherited retinal dystrophies. Only these dystrophies were taken into account that affected >10 patients and that fell into the two categories represented in fig. 1.

Table 1

Frequency of Different Genetic Forms of Retinitis Pigmentosa

Country	Year	Number of Cases	Dominant	Recessive	X-linked	Simplex	Reference
USSR	1969	678	1.1	12.7	–	27.9	Panteleeva 1969
Japan	1971	1,091	2.1	40.0	–	43.2	Imaizumi 1971
Japan	1972	1,650	–	54.6	–	–	Tanabe 1972
Japan	1972	839	–	64.7	–	–	Tanabe 1972
USA	1976	68	5.9	13.2	7.4	73.5	Pearlman et al. 1976
USA	1979	250	11.0	21.0	5.0	63.0	Pearlman 1979
USA	1980	670	10.0	69.0	6.0	15.0	Boughman et al. 1980
China	1982	151	11.0	33.4	7.7	48.3	Hu 1982
UK	1982	1,154	24.4	15.7	17.9	42.0	Jay 1982a
USA	1983	300	21.9	16.0	9.0	50.0	Boughman and Fishman 1982
USA	1984	168	43.4	19.6	7.7	29.2	Bunker et al. 1984
Norway	1986	407	16.4	52.1	5.5	26.0	Grondahl 1986
USA	1988	609	16.9	30.8	10.1	42.2	Heckenlively 1988
Australia	1989	707	27.3	27.1	10.3	38.0	Dickinson and Mulhall 1989
USSR	1990	2,000	12.0	39.2	2.2	46.6	Katznelson et al. 1990
France	1991	1,038	35.6	18.5	6.4	38.8	Puech et al. 1991
The Netherlands	1992	575	22.4	30.1	10.4	37.1	Van Den Born et al. 1992

Prevalence of both peripheral and choroidal retinal dystrophies is 1:2,705 and is 1:8,627 in patients with Stargardt's disease. The overall figure of the surveyed cases corresponds to a prevalence of 1:1,490 (table 2).

Those are high figures as compared to similar studies based on reasoned surveys in the world since 1961 (François 1961; Ammann et al. 1965; Panteleeva 1969; Imaizumi 1971; Tanabe 1972; Merin and Auerbach 1976; Pearlman 1979; Boughman et al. 1980; Hu 1982; Jay 1982*b*; Bunker et al. 1984; Newsome and Blacharski 1988; Heckenlively 1988; Dickinson and Mulhall 1989; Puech et al. 1991; Van Den Born et al. 1992) (tables 1 and 3). Most of the studies bore only on retinitis pigmentosa and choroidopathies. The latest surveys were made in countries - USA (Heckenlively 1988), Australia (Dickinson and Mulhall 1989), France (Puech et al. 1991), and The Netherlands (Van Den Born et al. 1992) - where over 90% of the population is of Caucasian descent. These surveys give identical or almost identical figures to those found in Northern France on the distribution of the different modes of transmission of retinitis pigmentosa (table 1). Though consanguinity does vary from one population to another, it has been assumed, within the framework of this study, that an equal structure can be found among these populations characterized by an almost exclusively Caucasian descent.

Table 2
Prevalence of the Main Inherited Retinal Dystrophies

Retinal Dystrophy	No Observed	Annual Incidence	No Estimated	Estimated Incidence	Prevalence (1/....)
Peripheral					
Retinitis pigmentosa	584	32.61	931	23.67	4,225
Cone-rod dystrophy	111	6.17	176	4.48	22,341
Leber's disease	41	2.28	65	1.65	60,485
Usher's syndrome	36	2.00	57	1.45	68,886
Bardet-Biedl's syndrome	23	1.28	36	0.93	107,822
Lipofuscinosis	22	1.22	35	0.89	112,723
Vitreoretinopathy	21	1.17	33	0.85	118,090
Congenital nyctalopia	20	1.11	32	0.81	123,995
Choroidal diseases	38	2.11	56	1.43	70,048
Choroideremia	15	0.83	22	0.56	177,454
Gyrate atrophy	13	0.72	19	0.49	204,754
Macular					
Stargardt's disease	286	15.90	431	10.91	8,627
X-linked retinoschisis	93	5.17	140	3.55	28,092
Cone dystrophy	33	1.80	48	1.22	81,937
Flavimaculated diseases	31	1.72	47	1.19	83,680
Best's disease	106	5.89	175	4.45	22,483
Gass's disease	51	2.83	84	2.14	46,729
Total	1,660	92.22	2,639	67.28	1,490

Table 3
Prevalence of Retinitis Pigmentosa and Allied Diseases

Country	Year	Prevalence (1/.....)	Reference
Switzerland	1965	7,000	Ammann et al. 1965
Israel	1976	2,000	Mérin and Auerbach 1976
USA	1980	2,500	Boughman et al. 1980
China	1982	4,016	Hu 1982
USA	1984	3,544	Bunker et al. 1984
Australia	1985	2,450	Cockburn 1985
France	1991	2,705	Puech et al. 1991

The possibility of an equal structure enables us to assess the range of this phenomenon on a European scale. Whereas at one extreme end, Germany counts 47,000 affected inhabitants out of a population of 78 million, at the other end, Vatican, with a population of approximately 1,000 inhabitants, seems to be statistically spared (table 4). For the whole Europe, we must assess that 300,000 people are affected, which justifies a common research project among all the Europeans and the implementation of specific structures within the European Community.

Table 4
Inherited Retinal Dystrophies in Europe

Country	Thousands of inhabitants	Retinal peripheral	Choroidal Peripheral	Macular Retinal	Pigmented Epithelium	Total
Albania	3140	1091	78	530	207	1906
Andorra	50	17	1	8	3	29
Austria	7600	2639	188	1282	501	4610
Belgium	9918	3445	246	1673	654	6018
Bulgaria	8981	3119	223	1515	592	5449
Czechoslovakia	15608	5421	387	2633	1029	9470
Denmark	5130	1782	127	865	338	3112
Finland	4950	1719	123	835	326	3003
France	55870	19404	1386	9425	3682	33897
Germany	77836	27032	1930	13131	5129	47222
Greece	9990	3470	248	1685	658	6061
Hungary	10597	3680	263	1788	698	6429
Iceland	250	87	6	42	16	151
Ireland	3540	1229	88	597	233	2147
Italy	57440	19949	1425	9690	3785	34849
Lichtenstein	30	10	1	5	2	18
Lithuania	3751	1303	93	633	247	2276
Luxembourg	370	129	9	62	24	224
Malta	340	118	8	57	22	205
Monaco	30	10	1	5	2	18
Netherlands	14760	5126	366	2490	973	8955
Norway	4210	1462	104	710	277	2553
Poland	37862	13149	939	6387	2495	22970
Portugal	10410	3615	258	1756	686	6315
Rumania	22940	7967	569	3870	1512	13918
San Marino	23	8	1	4	2	15
Spain	38830	13486	963	6551	2559	23559
Sweden	8440	2931	209	1424	556	5120
Switzerland	6550	2275	162	1105	432	3974
United Kingdom	57080	19824	1416	9629	3762	34631
Vatican	1	0	0	0	0	0
Yugoslavia	23560	8182	584	3975	1553	14294
Europe	500087	173679	12402	84362	32955	303398

This work shows that the frequencies of inherited retinal dystrophies calculated on the basis of epidemiological studies are most probably underestimated and that this frequency sets a real public health question.

References

- Ammann F**, Klein O, Franceschetti A (1965) Genetic and epidemiological investigations on pigmentary degeneration of the retina and allied disorders in Switzerland. *J Neurol Sci* 2:183-196
- Boughman JA**, Conneally PM, Nance WE (1980) Population genetic studies of retinitis pigmentosa. *Amer J Hum Genet* 32:223
- Boughman JA**, Fishman GA (-1982) A genetic analysis of retinitis pigmentosa. *Brit J Ophthalmol* 66:405-416
- Bunker CH**, Berson EL, Bromley WC, Hayes RP, and Roderick TH (1984) Prevalence of retinitis pigmentosa in Maine. *Amer J Ophthalmol* 97:357-365
- Cockburn DM** (1985) Retinitis pigmentosa: a review of the tapeto-retinal dystrophies. *Aust J Ophthalmol* 68:139-143
- Dickinson P**, Mulhall L (1989) A survey of hereditary aspects of pigmentary retinal dystrophies. *Aust N Z J Ophthalmol* 17:247-256
- Duke-Elder S**, Dobree JH (1967) Diseases of the retina. In: Duke-Elder S (ed). *System of ophthalmology*. C.V. Mosby, St Louis, pp 441-455
- Fishmann GA** (1978) Retinitis pigmentosa: genetic percentages. *Arch Ophthalmol* 96:822
- François J** (1961) Hereditary tapetoretinal degenerations. In: *Heredity in ophthalmology*. C.V. Mosby, St Louis, pp 441-455
- Grondahl J** (1986) Tapeto-retinal degeneration in four Norwegian counties: diagnostic evaluation of 407 relatives and genetic evaluation of 87 families. *Clin Genet* 9: 17-41
- Heckenlively JR** (1988) *Retinitis pigmentosa*. J.B. Lippincott, Philadelphia
- Hu D** (1982) Genetics aspects of retinitis pigmentosa in China. *Amer J Med Genet* 12:51
- Imaizumi K** (1971) Statistical investigation on retinitis pigmentosa. *Jpn J Clin Ophthalmol*. 25:293-304
- Jay M** (1982a) On the heredity of retinitis pigmentosa. *Brit J Ophthalmol* 66:405-416
- Jay M** (1982b) Figures and fantasies: the frequencies of the different genetics forms of retinitis pigmentosa. *Birth defects. Original Articles Series* 18:167-173
- Katznelson LA**, Khoroshilova-Maslova LP, Eliseyeva RP (1990) A new method of treatment of retinitis pigmentosa/pigmentary abiotrophy. *Ann Ophthalmol* 22: 167-172
- Merin A**, Auerbach E (1976) Retinitis pigmentosa. *Surv Ophthalmol* 20:303
- Newsome DA**, Blacharski P (1988) Fundus flavimaculatus and retinitis pigmentosa. In: *retinal diseases*. J.B. Lippincott, Philadelphia
- Panteleeva QA** (1969) On hereditary tapetoretinal degeneration (Russia). *Vesti Oftalmol* 8:53-56
- Pearlman JT** (1979) Mathematical models of retinitis pigmentosa: a study of the rate of progress in the different genetic forms. *Trans Amer Ophthalmol Soc* 77:643-656
- Pearlman JT**, Flood TP, Seiff SR (1976) Retinitis pigmentosa without pigment. *Amer J Ophthalmol* 81 :417-419
- Puech B**, Kostrubiec B, Hache J-C, François P (1991) Epidémiologie et prévalence des principales dystrophies rétinienues héréditaires dans le Nord de la France. *J F Ophtalmol* 14:153-164
- Tanabe U** (1972) Genetic study of retinal pigmentary dystrophy (retinitis pigmentosa) in Japan. *Jinrui Idengaku Zasshi* 16:119-154
- Van Den Born LI**, Bergen AAB, Bleeker-Wagemakers EM (1992) A retrospective study of registered retinitis pigmentosa patients in the Netherlands. *Ophthalmol Pediat Genet* 13:227-236



Vilnius 1994 - The workshop